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BIOLOGICAL TRANSFER OF PLUTONIUM VIA IN VIVO LABELED GOAT'S MILK

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Ecological Research Series

BIOLOGICAL TRANSFER OF PLUTONIUM VIA *IN VIVO* LABELED GOAT'S MILK

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16. ABSTRACT

Three lactating goats were given intravenous injections of citrate-buffered plutonium nitrate at a rate of 75 microcuries per animal per day for 3 consecutive days. Two goats received plutonium-238 and one received plutonium-239. The goats were hand milked at 8-hour intervals and portions of milk were 1) fed to juvenile goats, 2) fed to adult and juvenile rats, and 3) analyzed for plutonium content. Five days after dosing, one plutonium-238 injected goat was sacrificed and the remaining two goats were sacrificed 28 days after dosing. In all three goats approximately one percent of the total plutonium dose was transferred to the milk by the fifth post-treatment day. Plutonium retained by the tissues was deposited primarily in the liver and bone.

In vitro plutonium-labeled milk was also fed to groups of rats and juvenile goats. Tissue concentrations of plutonium from juvenile goats which had received either *in vivo* or *in vitro* labeled milk were somewhat variable. Due possibly to this, within group variability and the small number of animals per group (two) there were no clearly discernible differences between treatments. The percentage of dose retained in liver and carcass (pelt and gastrointestinal tract removed) of adult and juvenile rats was also compared after receiving the various plutonium doses. The only comparison point to show a consistent trend was the observation that, as expected, juvenile rats retained more of the ingested dose than the adult animals.

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CONCLUSIONS

1. Plutonium concentrations in goat milk have shown that approximately one percent of the intravenous dose (citrate-buffered plutonium nitrate, pH 4) was secreted in the milk during the first week post-injection. No differences in the plutonium transfer rate to milk were noted between plutonium-238 and plutonium-239.

2. There was little or no indication of basic differences in the amount of plutonium retained in the tissues of juvenile goats and rats following ingestion of either *in vivo* or *in vitro* plutonium labeled milk.

3. As expected, juvenile rats retained a greater percentage of the orally administered plutonium in the tissues than did the adult rats. This retention difference was noted for both plutonium-238 and for plutonium-239.

RECOMMENDATIONS

Nutritional factors affecting the biological availability of ingested plutonium should be determined by future experiments. *In vitro* and *in vivo* projects should assess gastrointestinal absorption of plutonium as affected by 1) mineral constituents, 2) complexing or binding factors, and possibly, 3) vitamin deficiencies. This is especially important in regard to potential variations in intestinal uptake, tissue distribution and subsequent excretion of ingested plutonium in laboratory and domestic animals as effected by chronic states of iron deficiency and iron loading.

INTRODUCTION

It is anticipated that with the increased use of nuclear power systems plutonium will be produced in greater quantities and could present a major health and ecosystem hazard. The long physical and biological half-life and high relative toxicity have dictated that considerable effort be devoted to quantifying plutonium transport through the various trophic levels.

Despite the fact that biological transport of plutonium has been studied for many years, quantitative values for its transfer to milk, and its subsequent uptake by suckling animals have not been established. In an early plutonium metabolism study on rats, Scott *et al.* (1948) observed that the average value for gastrointestinal absorption of plutonium using three different valence states was approximately 7.0×10^{-3} percent. Comparative studies on the intestinal uptake of plutonium nitrate revealed no significant differences in total absorption between the rat and pig (Weeks *et al.*, 1956). These results were quantitatively similar to those obtained in a rather extensive report by Katz *et al.* (1955) which, following a chronic oral plutonium treatment to rats, presented the mean gastrointestinal absorption and retention value at 3.0×10^{-3} percent of the administered dose.

While investigating the effects of plutonium on mice treated *in utero*, Finkel (1947) discussed the relative concentrations of this element which had been transported across the placenta or through the milk following parturition. Despite the early realization that plutonium could be transported via the systemic circulation to milk, essentially no work was reported on the major milk producers, i.e., ruminants. In 1964 Sansom studied the transfer of ingested plutonium oxide to bovine milk but observed that the results may have been influenced by fecal contamination. McClellan *et al.* (1962) injected two Suffolk sheep with citrate-buffered plutonium nitrate in order to establish a milk to plasma ratio. Although this study with sheep presented a milk to plasma reduction factor of 2.5×10^{-2}, it did not make reference to the subsequent biological availability of this *in vivo* plutonium labeled milk when ingested by juvenile animals. However, Ballou (1958) had previously reported that in day-old rats plutonium absorption was 85 times that in the adults and that the amount absorbed dropped abruptly in 21-day-old rats to near adult levels.

The basis for this study is that man and especially children consume large quantities of dairy products so that any evaluation of radiological hazards associated with a plutonium contaminated environment must consider the biological availability of *in vivo* plutonium labeled milk. The investigation was therefore designed to establish the rate of plutonium-238 and plutonium-239 transport to milk in the dairy goat. Furthermore, the study was conducted to provide order of magnitude comparisons on the biological availability of *in vivo* and *in vitro* plutonium labeled milk, as well as to observe the effect of animal age on the gastrointestinal uptake of the plutonium doses. Resulting information will be of value in designing definitive projects using dairy cattle. The use of both a ruminant and a rodent species will also be advantageous if subsequent extrapolations are made to other mammals, as in the case of plutonium transport models.

MATERIALS AND METHODS

Three adult lactating goats (mean weight 49 kg) were maintained in specially constructed metabolism stalls. Citrate-buffered plutonium nitrate was administered to the goats intravenously in doses of 75 μCi per animal per day for three consecutive days. Prior to the intravenous dosing, a sample of known activity was removed from a stock solution of plutonium nitrate and made up to volume with a citrate buffer. Approximately 3 ml of the resulting solution (pH 4) was then aspirated into a 5-ml syringe for injection. Two goats received plutonium-238 and one goat received plutonium-239. Blood samples, subquently separated into serum and formed elements, were collected from each animal daily. Five days after dosing one plutonium-238 injected goat was sacrificed by anesthetic overdose. The remaining two goats were sacrificed 28 days after dosing. Samples of liver, bone, muscle, kidney, spleen and blood were collected for analysis.

During this study the goats were hand-milked at eight-hour intervals and portions of milk were 1) fed to juvenile goats, 2) fed to adult and juvenile rats, and 3) analyzed for plutonium content. *In vitro* plutonium labeled milk was also fed to separate groups of juvenile goats and rats. The *in vitro* labeled milk was prepared by the addition of citrate-buffered plutonium nitrate to uncontaminated goat's milk. This *in vitro* preparation was thoroughly shaken and samples were removed for plutonium analysis just prior to dosing the kids and rats.

Four juvenile goats, one to three weeks of age with a mean weight of approximately 5 kg, received the oral doses of either the *in vivo* plutonium-238 labeled milk taken from the adult goat or the *in vitro* plutonium-238 labeled milk adjusted to the same plutonium concentration as the *in vivo* labeled milk. Dosing was accomplished with a bottle and nipple three times a day for four consecutive days (plate 1). The four juvenile goats were sacrificed on the third post-treatment day at which time samples of liver, bone, kidney, spleen and blood were taken.

Groups of adult and juvenile (12 to 14 days old) Wistar rats were given a series of either plutonium-238 *in vivo* labeled, plutonium-238 *in vitro* labeled, plutonium-239 *in vivo* labeled, or plutonium-239 *in vitro* labeled milk. Control animals received a placebo series of uncontaminated goat's milk. A dosing syringe with an appropriate needle modification was used to feed the rats (plate 2). Synthetic rat's milk would probably have been more nutritionally balanced for these rodents, however, supplemental rat feed and water were provided. Dosing took place three times a day for four consecutive days, therefore a total of 12 individual doses was given to each animal. In addition to the four basic treatment categories there was also a division within each treatment group based on the total concentration of plutonium administered. One subgroup was given essentially two times (2x) as

Plate 1. Dosing of juvenile goats using a bottle and nipple.

Plate 2. Dosing of rats using a syringe and appropriate needle modification.

much total plutonium as the other subgroup (x). The 2x treatment rats received either portions of the milk secreted by the plutonium-injected adult goats or an *in vitro* preparation equal in plutonium concentration to the *in vivo* labeled milk. The x treatment groups received milk with one half the secreted plutonium concentration as each x dose consisted of an equal volume of contaminated milk and uncontaminated goat's milk. As mentioned above, control rats received uncontaminated goat's milk.

Rat breeding cages with solid bottoms containing wood shavings as bedding material were used for the juvenile rats while adult rats were maintained in mesh bottom cages over trays containing absorbent paper. Bedding material and absorbent paper were changed every second day throughout the study. Groups of adult rats were sacrificed at day 2 and day 7 after the dosing sequence was completed. Juvenile rats were originally scheduled to be sacrificed at these time intervals, however, all juveniles were sacrificed on post-treatment day 2 because of some unexpected juvenile deaths. The liver and the carcass of each rat were

collected at time of sacrifice. Pelts and gastrointestinal tracts, which might have been contaminated with unabsorbed plutonium, were carefully removed and discarded (plate 3).

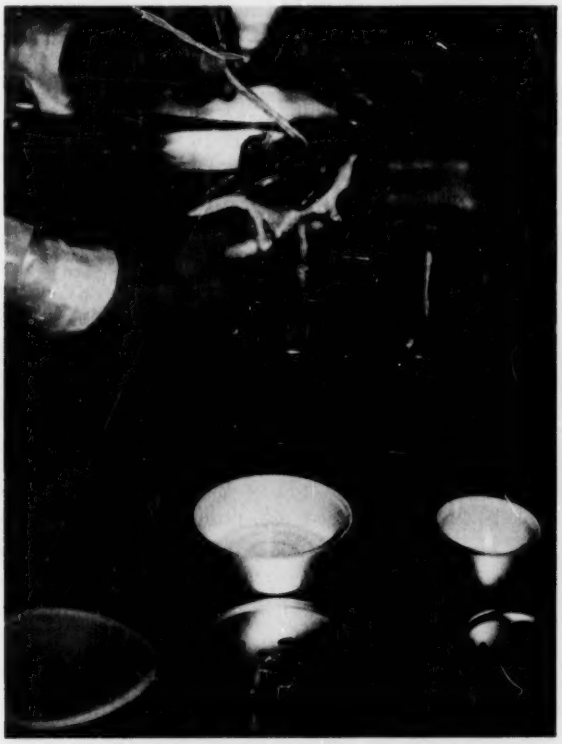

Plate 3. Rat sacrifice illustrating the technique used to remove the pelt from the carcass.

Rat carcasses and livers were analyzed for plutonium content by means of electrodeposition and alpha spectrometric analysis. At time of analysis, whole samples were dry-ashed in a muffle furnace at a maximum temperature of 550° C, then dissolved in 8 N nitric acid and spiked with a tracer isotope (^{242}Pu for ^{238}Pu samples and ^{236}Pu for ^{239}Pu samples). Samples were wet-ashed to remove organic material, the ash was redissolved, and the valence adjusted to plutonium (IV). Following an extraction and back-extraction procedure, the samples were electroplated and counted on an alpha spectrometer.

The other samples (goat tissues, milk, blood, etc.) were counted on a Phoswich detector provided with a single channel analyzer, timer, scaler and printout set for the 17 KeV x-ray from the plutonium isotopes. The system was calibrated for each geometry and the concentrations were considered to be nondetectable when the counting error (background plus 2 σ) reached 30 percent. Duplicate samples of milk were taken at each collection and both sets were counted periodically.

RESULTS AND DISCUSSION

Plutonium tissue distribution patterns in the intravenously injected adult goats were basically similar to the tissue patterns reported in other species (Rosenthal *et al.*, 1972). As noted in Table 1, the plutonium-238 concentrations in liver substantially decreased between sacrifice day 5 and 28, while bone concentrations of plutonium-238 showed an increase during this interval. Since only portions of the skeleton were analyzed, some assumptions were made in order to estimate the total osseous retention. For the purposes of this study, plutonium concentrations from goat rib and femur samples were averaged to arrive at bone concentrations. Total plutonium content in bone, as well as that for muscle and blood, were measured based on calculated organ weights using the respective percentage of body weight reported by Davis *et al.*, 1975.

Variations in the osseous burdens between the plutonium-238 and plutonium-239 dosed animals (noted at the 28-day sacrifice, Table 1) were fairly large. The main non-experimental difference in these two goats was the wide range in animal age. Considering the close resemblance of the other retention values, as well as the plutonium concentrations in milk, it appears unlikely that the observed bone burden differences indicate a basic variation in the general deposition pattern following administration of these two plutonium isotopes.

For comparative purposes, the percentage of plutonium retained in the tissues of a lactating goat following an acute dose of 50 μCi plutonium-238 is shown in Table 2. This information was taken from an unpublished preliminary study by Stanley and Mullen (1971). Citrate buffer was added to plutonium nitrate and the resulting solution (pH 4) was injected intravenously. The goat was sacrificed 30 days after dosing. As with the three goats used in the current study, the largest percentage of plutonium was retained in the liver and values for the spleen and muscle were also comparable. However, the fraction retained in bone after the single injection was lower than expected. Plutonium transported to milk as a result of the acute injection is presented in Figure 1 as a percent of dose per ml of milk. The total secretion of plutonium in milk 18 days following injection was approximately one percent of the acute dose.

Plutonium concentration in the systemic circulation is a primary physiological variable influencing subsequent transfer to milk. An indication of this was found during the dosing days and during the first three post-treatment days (Figures 2, 3, and 4). Figure 5 shows the comparative total nCi of plutonium secreted in the milk for these

TABLE 1. PERCENT OF TOTAL INTRAVENOUS PLUTONIUM DOSE RETAINED IN SELECTED TISSUES FROM LACTATING DAIRY GOATS THAT RECEIVED 75 μCi OF CITRATE-BUFFERED PLUTONIUM PER ANIMAL PER DAY FOR THREE CONSECUTIVE DAYS

Adult Goat No.	1	2	3
Plutonium Isotope	^{238}Pu	^{238}Pu	^{239}Pu
Total I.V. Dose (μCi) (buffered in citrate)	225	225	225
Sacrifice Weight (kg)	44.6	45.9	50.9
Animal Age (y)	4	2	10
Sacrifice Time (days post treatment)	5	28	28
Average Daily Milk Production (kg)			
8 day average	4.6	3.0	1.3
30 day average		2.7	2.6
Percentage of Total Dose Secreted in Milk			
128 h post	1.0	1.6	1.0
672 h post		2.0	1.1
Biological Half-Life of Plutonium in Milk (h)		9.28 ± 1.85 108 ± 13.3 >656	12.6 ± 1.57 84.2 ± 9.34 >700
Percentage of Total Dose Retained in Tissues			
Blood	9.0×10^{-2}	1.0×10^{-1}	4.0×10^{-1}
Liver	53.6	14.0	13.2
Muscle	8.0×10^{-1}	1.0	1.2
Kidney	2.0×10^{-1}	1.2×10^{-1}	4.0×10^{-1}
Spleen	3.0×10^{-2}	8.0×10^{-2}	9.0×10^{-2}
Bone	6.0	13.2	1.0

TABLE 2. PERCENT OF INTRAVENOUS PLUTONIUM DOSE RETAINED IN SELECTED TISSUES FROM LACTATING DAIRY GOATS THIRTY DAYS AFTER RECEIVING 50 μCi OF CITRATE-BUFFERED PLUTONIUM-238

Tissue	pCi/g	Percent of Dose Retained
Muscle	32.4	1.3
Bone	58.7	4.4×10^{-1}
Liver	15.0×10^{3}	25.0
Lungs	96.5	7.2×10^{-2}
Heart	82.6	3.4×10^{-2}
Brain	157.0	3.8×10^{-2}
Spleen	147.1	3.2×10^{-2}

goats. There were slightly different plutonium concentrations at peak activity as well as variations in the time to peak activity between the three goats. The obvious complicating factors of biological variability between animals, counting error, the multiple dose type of treatment, and the sampling interval suggest that a detailed comparative analysis of the plutonium secretion curves for milk would be of doubtful significance. However, the percentage of total dose secreted in the milk 176 hours after the initial plutonium dose (128 hours post-treatment) was 1.0, 1.6 and 1.0 for the two plutonium-238 injected goats and the one plutonium-239 injected goat, respectively. Biological half times for plutonium in the milk fraction are presented in Table 1.

As indicated in Table 3, the total oral dose given to the four juvenile goats falls generally into two dose levels. These two sets exist (kid 1 and 3, plus kid 2 and 4) because kids 1 and 2 were given *in vivo* labeled milk from different adult goats, and therefore received different amounts of plutonium per ml of milk ingested. As mentioned earlier, kids 3 and 4 received *in vitro* labeled milk essentially equal in plutonium concentration to that received by kids 1 and 2. Since the dose was not adjusted to animal weight (nCi/kg) these two dosage levels are by no means clear separations. However, the percentage of plutonium retained in selected tissues is given for each individual animal.

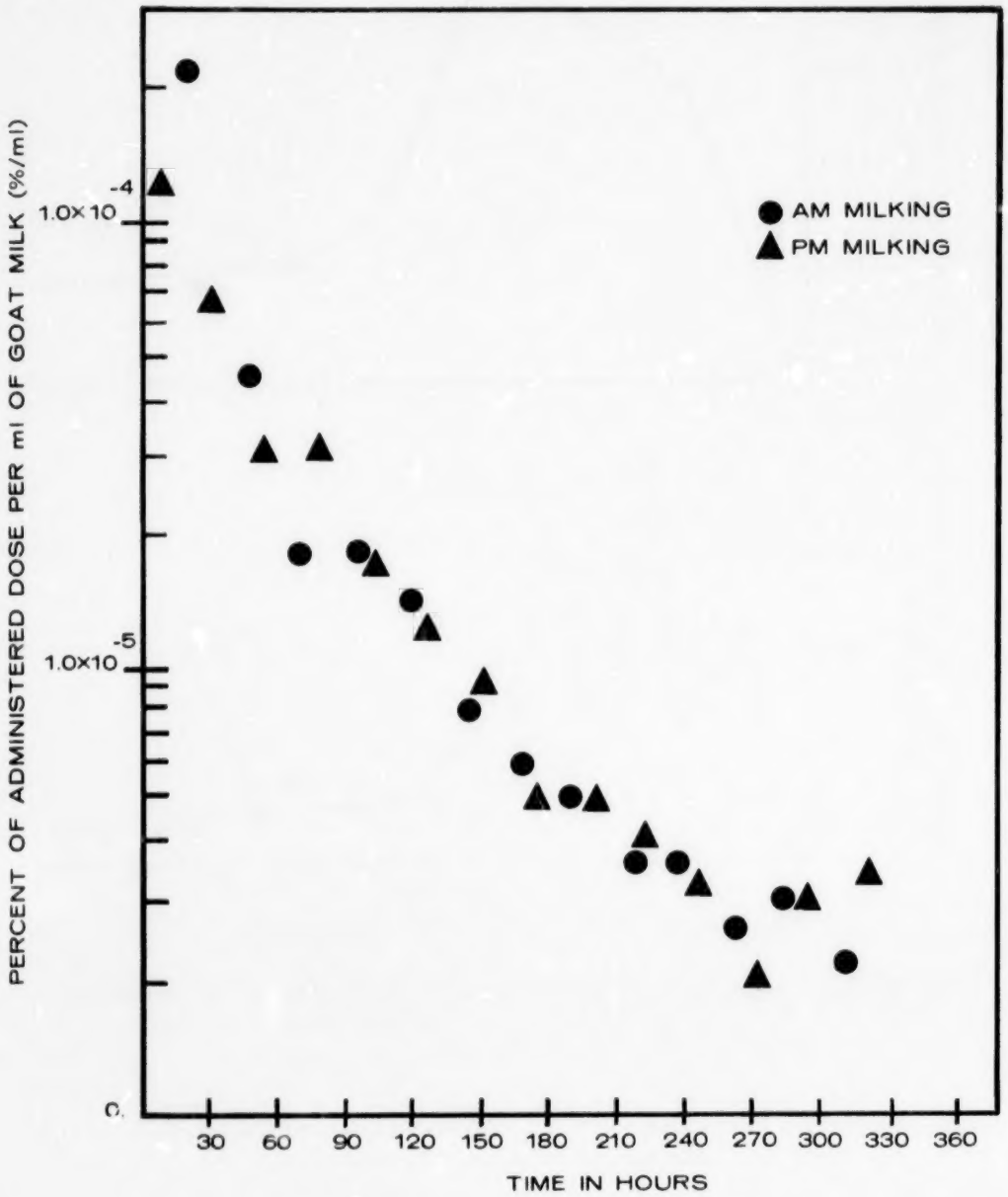

Figure 1. Concentration of plutonium in goat milk following a single intravenous injection of citrate-buffered plutonium-238

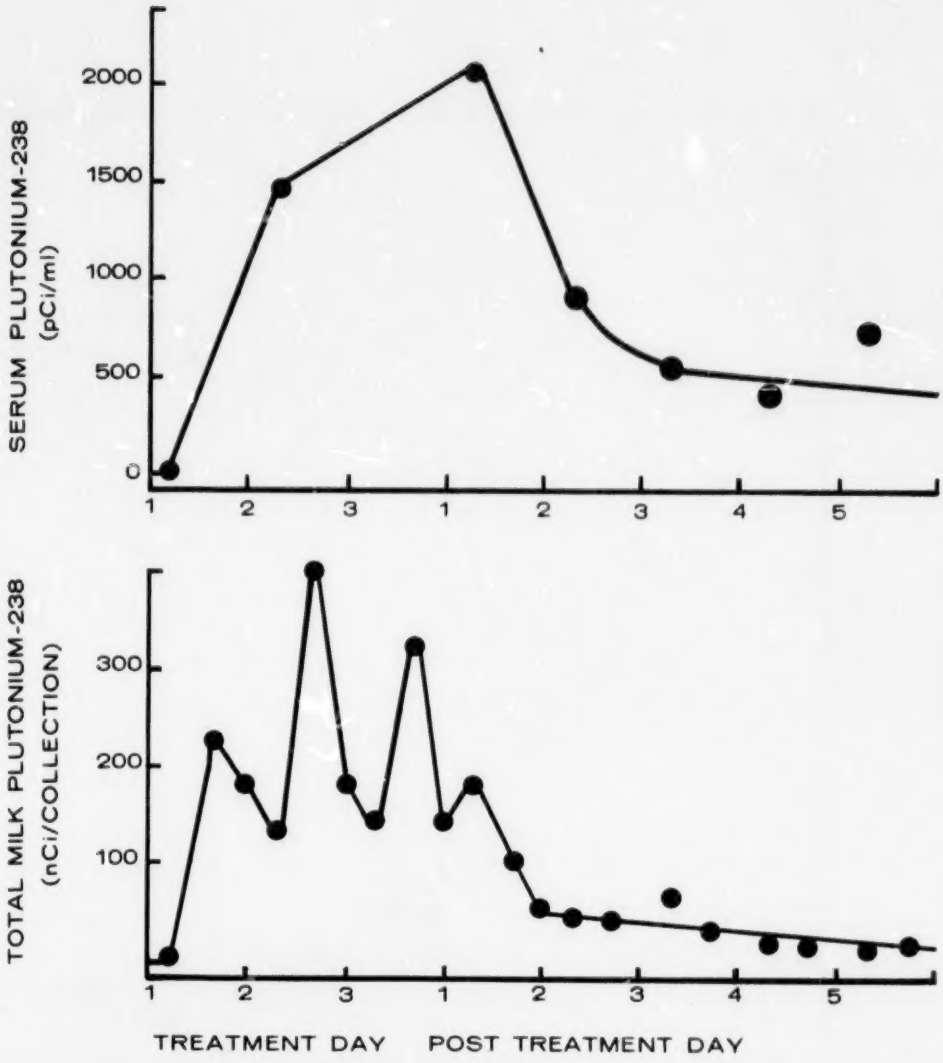

Figure 2. Comparison between serum and milk plutonium following intravenous injections of plutonium-238 on three consecutive days (goat 1)

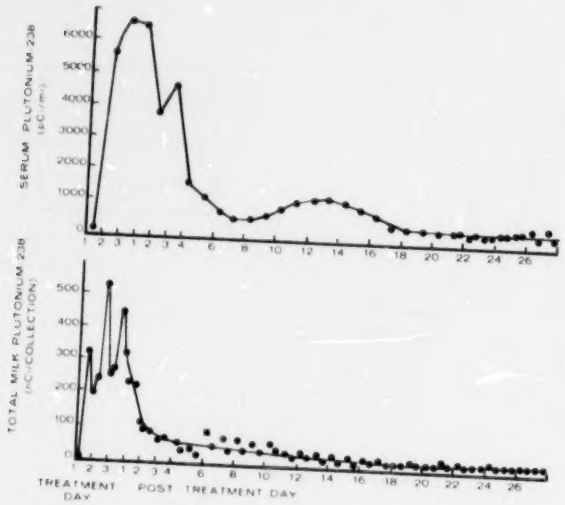

Figure 3. Comparison between serum and milk plutonium following intravenous injections of plutonium-238 on three consecutive days (goat 2)

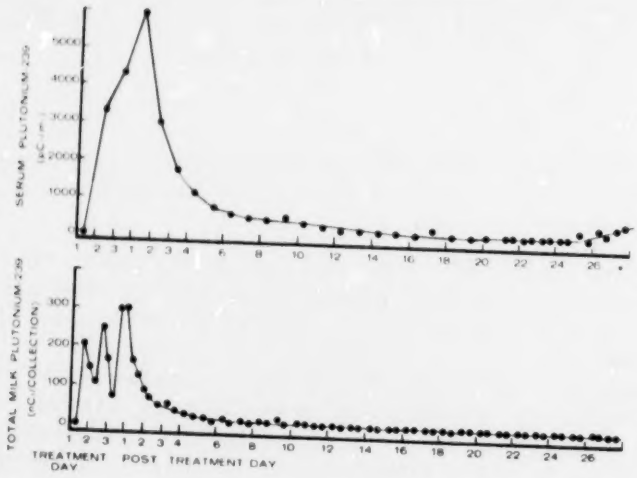

Figure 4. Comparison between serum and milk plutonium following intravenous injections of plutonium-239 on three consecutive days

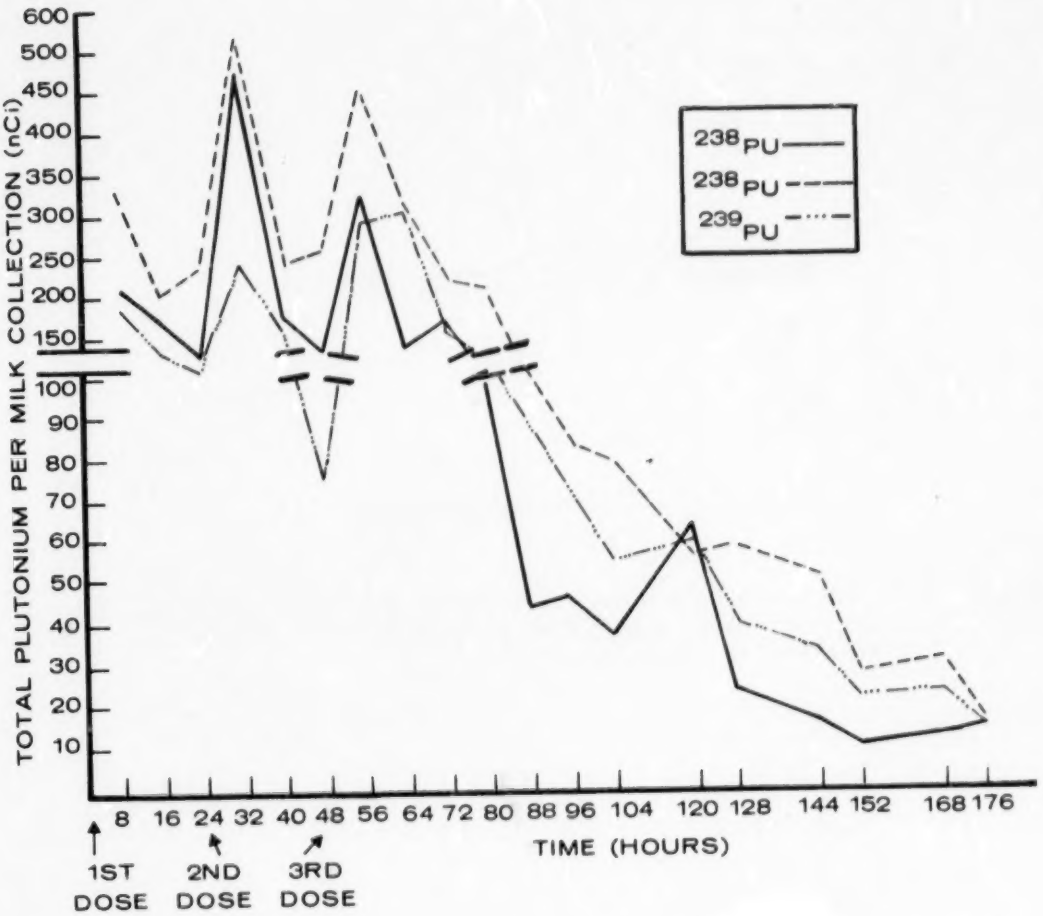

Figure 5. Total plutonium (nCi) in milk collections from three goats intravenously administered 75 µCi of plutonium per day for three consecutive days

If liver and bone had been the only kid tissues analyzed, there might have been a suggestion of greater retention in the *in vivo* labeled group. There was also a suggestion of greater retention for juvenile goats which received the high plutonium dose, irrespective of *in vivo* or *in vitro* preparation. However, within-group variability in plutonium concentrations for the kid tissues was great in both groups on a pCi/g of sample basis. Extrapolations to a percentage of dose retained per organ obscure this variability somewhat and further studies with larger numbers of kids are probably necessary before final conclusions are reached. Based on all juvenile goat tissues analyzed during this study, there seems to be no clearly discernible difference in the total intestinal absorption of *in vivo* and *in vitro* labeled milk, nor in the gross tissue deposition pattern following these respective treatments.

TABLE 3. PERCENT OF TOTAL PLUTONIUM DOSE RETAINED IN SELECTED TISSUES FROM FOUR JUVENILE GOATS THAT RECEIVED THREE ORAL DOSES OF PLUTONIUM-238 CONTAMINATED MILK PER DAY FOR FOUR CONSECUTIVE DAYS

Juvenile Goat No.	*In Vivo* Labeled Milk		*In Vitro* Labeled Milk	
	1	2	3	4
Sacrifice weight (kg)	4.7	3.7	8.1	5.1
Total Oral ^{238}Pu Dose (nCi)	383	1008	388	1103
Age at Beginning of Study (days)	8	5	23	12
Percent of Total Dose Retained in Tissues (3 days post treatment)				
Blood	2.0×10^{-2}	2.0×10^{-2}	6.0×10^{-2}	7.0×10^{-2}
Liver	1.0×10^{-1}	3.0×10^{-1}	5.0×10^{-2}	9.0×10^{-2}
Kidney	2.0×10^{-2}	5.0×10^{-2}	3.0×10^{-2}	6.0×10^{-2}
Spleen	1.0×10^{-2}	1.0×10^{-2}	2.0×10^{-2}	6.0×10^{-1}
Bone	5.0×10^{-1}	1.0	2.0×10^{-1}	6.0×10^{-1}

Rats were also studied during the project for purposes of comparison and because each dosing sequence could be administered to larger numbers of these laboratory animals. Table 4 shows the mean percent of dose retained in liver and carcass (pelt and gastrointestinal tract removed) from adult rats that received the complete dosing sequence. Italicized values (alternate rows) indicate that groups of adult rats were sacrificed seven days after termination of the oral plutonium dosing. The other adult rats were sacrificed two days after dosing. Values for juvenile rats are given in Table 5, but in this case all animals were sacrificed approximately two days post-treatment. A total of 12 individual doses was given to each animal and the average total dose is also indicated in these tables. An average total dose was used since there were occasional slight variations in the amount actually ingested and the doses were not adjusted to the individual rat weights. In addition to the basic treatment categories there was also a division of animals based on the total concentration of plutonium administered and it will be recalled that the study was designed to include two main subgroups per treatment, one of which would receive essentially two times more total plutonium than the other subgroup.

TABLE 4. MEAN PERCENT OF TOTAL PLUTONIUM DOSE RETAINED IN LIVER AND CARCASS FROM ADULT RATS THAT RECEIVED THREE ORAL DOSES OF PLUTONIUM CONTAMINATED MILK PER DAY FOR FOUR CONSECUTIVE DAYS

Treatment Group	No. of Animals	Mean Oral Dose (total pCi)	Mean Percent of Dose Retained in Tissues	
			Liver	Carcass
^{238}Pu *in vivo* labeled	6	3374	4.4×10^{-1}	2.4
	6	3352	*1.2×10^{-2}*	*3.7×10^{-2}*
	6	7068	2.3×10^{-3}	2.4×10^{-2}
	6	7006	*7.1×10^{-3}*	*2.3×10^{-2}*
^{238}Pu *in vitro* labeled	6	3708	7.6×10^{-1}	5.7
	6	3764	*1.3×10^{-3}*	*8.5×10^{-2}*
	6	7485	1.3×10^{-3}	5.3×10^{-2}
	6	7460	*1.8×10^{-3}*	*4.6×10^{-2}*
^{239}Pu *in vivo* labeled	5	4507	1.2×10^{-2}	1.4×10^{-2}
	5	4528	*9.7×10^{-3}*	*2.0×10^{-2}*
	6	9090	1.6×10^{-3}	1.3×10^{-2}
	6	9084	*2.4×10^{-3}*	*1.3×10^{-1}*
^{239}Pu *in vitro* labeled	6	5010	5.2×10^{-3}	5.6×10^{-2}*
	6	5010	*1.0×10^{-2}*	*2.0×10^{-2}*
	5	10024	7.5×10^{-2}	1.5×10^{-1}
	6	9997	*5.1×10^{-3}*	*2.4×10^{-2}*

NOTE: Italics = 7 day sacrifice
*Based on three rats

TABLE 5. MEAN PERCENT OF TOTAL PLUTONIUM DOSE RETAINED IN LIVER AND CARCASS FROM JUVENILE RATS THAT RECEIVED THREE ORAL DOSES OF PLUTONIUM CONTAMINATED MILK PER DAY FOR FOUR CONSECUTIVE DAYS

Treatment Group	No. of Animals	Mean Oral Dose (total pCi)	Mean Percent of Dose Retained in Tissues	
			Liver	Carcass
^{238}Pu *in vivo* labeled	7	897	5.0×10^{-1}	6.4
	9	1737	1.1	5.4
^{238}Pu *in vitro* labeled	9	942	6.1×10^{-1}	9.1
	10	1882	2.3×10^{-1}	4.1
^{239}Pu *in vivo* labeled	4	1137	5.5×10^{-1}	6.9
	5	2257	6.8×10^{-1}	7.0
^{239}Pu *in vitro* labeled	9	1251	2.8×10^{-1}	4.9
	5	2469	3.4×10^{-1}	5.1

Several specific points of comparison were therefore possible from the tissue retention information on adult and juvenile rats. As stated above, these comparisons include observations on the relative biological availability of (1) *in vivo* and *in vitro* plutonium labeled milk, (2) different plutonium concentrations ingested within a treatment group, (3) isotopic differences between plutonium-238 and plutonium-239, plus (4) differences in tissue retention as related to animal age. In adult rats, occasional order of magnitude retention differences were found after ingestion of the two respective plutonium isotopes as well as after ingestion of *in vivo* as compared to *in vitro* labeled milk. However, there was little indication of any basic change in overall plutonium availability. The only comparison point to show a consistent trend was the observation that, as expected, juvenile rats retained more of the administered dose than the adult animals. Comparisons between the percentage of plutonium retained in adult and juvenile rats can be made with the liver values at the two-day post-treatment sacrifice. The liver is a main initial deposition site of intestinally absorbed plutonium and the rat liver is a relatively easy organ to remove for analysis. At least one order of magnitude difference was usually noted between adult and juvenile livers, and

in several cases two orders of magnitude were observed. The percentage of the oral dose retained in juvenile rat carcasses appears high and it might be advantageous to analyze the lungs separately in future studies to determine if exposure was intratracheal rather than intragastric.

Livers and carcasses were analyzed for background determinations from control rats (12 adult and 12 juvenile) which had been maintained and sacrificed along with the treatment animals. Actually, the tissue concentrations in many of the dosed adult rats were at or only slightly above background on a pCi/g of sample basis, and the general level of plutonium retention in most of the dosed adult tissues was quite low. Percentages extrapolated from adult rats at or smaller than 10^{-4} would fall within the background range and values smaller than 10^{-2} were extrapolated as background levels for the juveniles.

Tables 4 and 5 represent a compromise approach to reporting values from this plutonium investigation. The tissue analyses for plutonium were conducted on an activity per gram basis not activity per organ. Furthermore, an individual aluminum can containing either rat liver or carcass samples frequently contained more than one liver or more than one carcass. When a can contained more than one sample, the samples were of course taken from animals which had received approximately equal doses of a given plutonium treatment and had been sacrificed at the same post-treatment time. However, the analytical sample size (for statistical comparisons, i.e., analysis of variance) would consequently be the number of aluminum cans analyzed per treatment, not the number of animals as implied in these summary tables.

The overall increased plutonium absorption noted in juvenile rats relative to adults was in agreement with the findings of other investigators. Ballou (1958) noted that in day-old rats the gastrointestinal absorption of plutonium (nitric acid solution) was 85 times that recorded for the adult. An average gastrointestinal absorption of plutonium nitrate for adult rats was reported by Weeks *et al.* (1956) to be 2.8×10^{-3} percent. However, detailed comparisons between plutonium tissue retention patterns in adult and juvenile animals are somewhat complicated by the size of individual organs relative to the total animal weight. For example, Sikov and Mahlum (1972) reported that skeletal weight in the rat was approximately 24 percent of body weight at birth, but dropped to 10 percent in the adult.

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